REMARKS

Claim 32 has been amended to change "any" back to "said." This is in direct response to the assertion of lack of priority and "new matter" rejection under 35 U.S.C. § 112, paragraph 1. As this is the first opportunity to respond to the new matter rejection, and the response obviates the rejection, applicants believe that entry of the amendment is proper at this time. Entry of the amendment is respectfully requested.

Applicants appreciate the acknowledgement of the terminal disclaimer and the withdrawal of the previous rejection under 35 U.S.C. § 112, paragraph 2.

Priority

With respect to claim 32, and therefore all claims dependent thereon, priority is questioned apparently because of the word "any" as opposed to "said" in the third to last line of the claim. The amendment has returned the wording to "said" so as to that aspect of denial of priority, this has been corrected.

In addition, the Office states that the portion of the specification at page 6, lines 5-13, regarding the construction of a library as set forth in claim 41 is applicable only to plants, and therefore the application is entitled only to its filing date. Applicants point out, however, that claim 11 filed originally with the parent application US 09/491,549 (now U.S. patent 6,753,139) filed 26 January 2000 referred to constructing a library from any organism. As the claims are part of the specification, as the Examiner here recognizes, there is support for this claim as of this filing date. In addition, this is supported at page 3, lines 30-38.

This denial of priority applies only to claim 41.

In any event, the priority accreditation is not germane to the outstanding rejections over the art.

Oath / Declaration

A new oath executed by the inventors accompanies this response.

The Art Rejections

Claims 32, 35-37, 39, 40, 47 and 49 were rejected as assertedly anticipated by Agrawal, *et al.* (WO 94/01550) as further evidenced by Bridge, *et al., Nature Genetics* (2003) 34:263-264.

Applicants have reviewed the rejection as originally made and have carefully reviewed the example in Agrawal cited by the Office. There appears to be nothing in this example that describes preparing any extracts at all of the infected cells. Apparently, the cells were tested for cell survival after administration of the test compounds and the supernatants were measured using an ELISA for p34 expression. There is no mention of any extraction, or of any analysis for the presence of any oligo or polynucleotides in any associated sample.

Thus, the explicit step in claim 32 of "analyzing a nucleic extract prepared from said organism to determine the presence or absence of short RNA molecules..." is missing, as is certainly the additional step of "characterizing" any SRMs present.

In addition, the citation of Bridge is inapposite because Bridge describes the processing of short hairpin RNA's that are generated from DNA vectors. Agrawal, in example 3, does not describe the administration of short hairpin RNA's, but rather the administration of hairpin DNA molecules (not vectors to generate RNA). The compounds used are shown in figure 5, all of which contain thymine bases rather than uracil bases, and are thus DNA not RNA.

If there is someplace in Agrawal where an extraction of a cell or organism undergoing gene silencing is analyzed for oligonucleotides or polynucleotides or where there is any characterization of such contents, applicants are unable to find it. Accordingly, this basis for rejection should be withdrawn.

Claims 32, 35, 36, 38, 40 and 47-49 were rejected as assertedly anticipated by Baracchini, *et al.* (US 5,801,154).

Applicants have reviewed the rejection as previously proposed, and still find no disclosure of the steps of analyzing a nucleic acid extract prepared from an organism to determine the presence or absence of short RNA molecules or of characterizing such short RNA molecules. The Office refers to column 6 as describing screening for the desired result cells that have putatively undergone gene silencing by virtue of antisense techniques. The only mention of such analysis in column 6 appears to be at lines 5-10 which suggest culturing and screening the cells for reversal of drug resistance – *i.e.*, increased sensitivity to chemotherapeutic drugs as quantitated by a decrease in the IC_{50} values. This does not sound to applicants like analyzing extracts for short RNA molecules.

The Office points to column 11 where Northern blots were obtained to determine the effects of certain antisense moieties added to the cells on "MRP mRNA levels." mRNA encoding MRP is not a short RNA molecule. The only assay described is directed to the level of this mRNA. This is clearly not the same or even anything resembling analyzing an extract for the presence or absence of short RNA molecules.

Indeed, as pointed out by applicants in their specification, on page 7 at line 10,

> "Regarding detection because of their small size, the method for this is not the usual one for 'RNA gel blot analysis' although the principle is the same, *i.e.*, separation of the RNA molecules according to size by electrophoresis through a gel."

And, as further pointed out on page 2 of the specification at lines 22, *et seq.*,

> There have been no previous reports of such short sense and antisense RNA molecules (hereafter, collectively SRMs) that are detected exclusively in organisms exhibiting PTGS, possibly because (owing to their size) they could not have been readily detected by routine RNA analyses.

The specification thus makes clear that unless one deliberately sets about to look for short RNA molecules, they would not be detected in routine RNA analysis, and certainly not in Northern blots designed simply to detect the levels of a specific mRNA.

Since Baracchini fails to set forth all of the steps required by the claim, it cannot anticipate the claims subject to this rejection.

The Rejection Under 35 U.S.C. § 112, Paragraph One (New Matter)

This basis for rejection has been obviated by amendment. While applicants do not really see the difference between "said" and "any" in regard to the scope of the claim or the subject matter being claimed, they are perfectly willing to change "any" back to "said." In reviewing the record, it is unclear why the change was made in the first place, possibly the antecedent basis for a target gene in line 2 of the claim was overlooked.

In any event, the amendment disposes of this rejection.

Claims 33 and 34

These claims were withdrawn from consideration as directed to non-elected species. They were not subject to a restriction requirement. Since claim 32, from which these claims depend, and which is generic, is in position for allowance, these claims may now be rejoined.

Conclusion

Claim 41 is not subject to any rejection over the art. It is apparently included in the new matter rejection only because it is dependent from claim 32. This basis for rejection has been remedied by amendment.

It has also been shown that claims 32, 35-37, 39-40, 47 and 49 are free of the cited art. Accordingly, examined claims 32, 35-37, 39-41, 47 and 49 are in a position for allowance and claims 33-34 may be rejoined. Passage of all pending claims to allowance is therefore respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 616292000110.

Respectfully submitted,

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By: Electronic signature: /Kate H. Murashige/
Kate H. Murashige
Registration No. 29,959
MORRISON & FOERSTER LLP
12531 High Bluff Drive
Suite 100
San Diego, California 92130-2040
Telephone: (858) 720-5112
Facsimile: (858) 720-5125